



SEQUENCE LISTING

<110> CHANG, Y-H
VETRO, J.A.
MICKA, W.S.

<120> DOMINANT NEGATIVE VARIANTS OF METHIONINE AMINOPEPTIDASE
2 ("METAP2") AND CLINICAL USES THEREFOR

<130> 2790/66153/8007

<140> 10/712,359

<141> 2003-11-13

<150> 09/943,123

<151> 2001-08-30

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<170> PatentIn Ver. 3.2

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Lys Lys Lys Ser Asn Val Lys Lys Ile
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Ser Gly Arg Ile Ile Xaa Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
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275 280 285
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Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
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Arg Xaa Xaa Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
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Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Xaa Thr Phe Gly Ser
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Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
370 375 380
Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
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His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
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Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
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Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys
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	35						40					45			
Val	Ser	Ala	Val	Gln	Gln	Glu	Leu	Asp	Lys	Glu	Ser	Gly	Ala	Leu	Val
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Asp	Glu	Val	Ala	Lys	Gln	Leu	Glu	Ser	Gln	Ala	Leu	Glu	Glu	Lys	Glu
65					70					75					80
Arg	Asp	Asp	Asp	Asp	Glu	Asp	Gly	Asp	Gly	Asp	Ala	Asp	Gly	Ala	Thr
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Gly	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Arg	Gly	Pro	Lys	Val	Gln
			100						105				110		
Thr	Asp	Pro	Pro	Ser	Val	Pro	Ile	Cys	Asp	Leu	Tyr	Pro	Asn	Gly	Val
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			260					265					270		
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 35 40 45
 Lys Lys Lys Lys Ser Asn Val Lys Lys Ile Glu Leu Leu Phe Pro Asp
 50 55 60
 Gly Lys Tyr Pro Glu Gly Ala Trp Met Asp Tyr His Gln Asp Phe Asn
 65 70 75 80
 Leu Gln Arg Thr Thr Asp Glu Glu Ser Arg Tyr Leu Lys Arg Asp Leu
 85 90 95
 Glu Arg Ala Glu His Trp Asn Asp Val Arg Lys Gly Ala Glu Ile His
 100 105 110

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Pro	Asn	Ala	Gly	Asp	Lys	Thr	Val	Leu	Lys	Tyr	Glu	Asp	Val	Met	Lys	180	185	190
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Thr	Val	Ser	Phe	Asp	Pro	Gln	Tyr	Asp	Asn	Leu	Leu	Ala	Ala	Val	Lys	210	215	220
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Ala	Ile	Xaa	Thr	Phe	Gly	Ser	Thr	Gly	Arg	Gly	Tyr	Val	Thr	Ala	Gly	305	310	315
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Pro	Thr	Leu	Asp	Ser	Ala	Lys	Asn	Leu	Leu	Lys	Thr	Ile	Asp	Arg	Asn	340	345	350
Phe	Gly	Thr	Leu	Pro	Phe	Cys	Arg	Arg	Tyr	Leu	Asp	Arg	Leu	Gly	Gln	355	360	365
Glu	Lys	Tyr	Leu	Phe	Ala	Leu	Asn	Asn	Leu	Val	Arg	His	Gly	Leu	Val	370	375	380
Gln	Asp	Xaa	Pro	Pro	Xaa	Asn	Asp	Ile	Pro	Gly	Ser	Tyr	Thr	Ala	Gln	385	390	395
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Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu
      65             70             75             80

Arg Asp Glu Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr
      85             90             95

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      100            105            110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
      115            120            125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
      130            135            140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
      145            150            155            160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
      165            170            175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
      180            185            190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
      195            200            205

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Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser
 210 215 220
 Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr
 225 230 235 240
 Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile
 245 250 255
 Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
 260 265 270
 Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
 275 280 285
 Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
 290 295 300
 Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
 305 310 315 320
 Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr
 325 330 335
 Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
 340 345 350
 Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser
 355 360 365
 Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
 370 375 380
 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
 385 390 395 400
 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
 405 410 415
 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
 420 425 430
 Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
 435 440 445
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<211> 478

<212> PRT

<213> Mus musculus

<220>

<223> Mouse MetAP2

<400> 13

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Asp	Leu	Asp	Pro	Asp	Asp	Arg	Glu	Glu	Gly	Thr	Ser	Ser	Thr	Ala	Glu	
			20					25					30			
Glu	Ala	Ala	Lys	Lys	Lys	Arg	Arg	Lys	Lys	Lys	Lys	Gly	Lys	Gly	Ala	
		35					40					45				
Val	Ser	Ala	Val	Gln	Gln	Glu	Leu	Asp	Lys	Glu	Ser	Gly	Ala	Leu	Val	
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65					70					75					80	
Arg	Asp	Asp	Asp	Asp	Glu	Asp	Gly	Asp	Gly	Asp	Ala	Asp	Gly	Ala	Thr	
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Gly	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Arg	Gly	Pro	Lys	Val	Gln	
			100					105					110			
Thr	Asp	Pro	Pro	Ser	Val	Pro	Ile	Cys	Asp	Leu	Tyr	Pro	Asn	Gly	Val	
	115						120					125				
Phe	Pro	Lys	Gly	Gln	Glu	Cys	Glu	Tyr	Pro	Pro	Thr	Gln	Asp	Gly	Arg	
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Thr	Ala	Ala	Trp	Arg	Thr	Thr	Ser	Glu	Glu	Lys	Lys	Ala	Leu	Asp	Gln	
145					150					155					160	
Ala	Ser	Glu	Glu	Ile	Trp	Asn	Asp	Phe	Arg	Glu	Ala	Ala	Glu	Ala	His	
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Arg	Gln	Val	Arg	Lys	Tyr	Val	Met	Ser	Trp	Ile	Lys	Pro	Gly	Met	Thr	
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	195						200					205				
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	210					215					220					
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225					230					235					240	
Val	Leu	Gln	Tyr	Asp	Asp	Ile	Cys	Lys	Ile	Asp	Phe	Gly	Thr	His	Ile	
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Ser	Gly	Arg	Ile	Ile	Asp	Cys	Ala	Phe	Thr	Val	Thr	Phe	Asn	Pro	Lys	
			260					265					270			
Tyr	Asp	Ile	Leu	Leu	Thr	Ala	Val	Lys	Asp	Ala	Thr	Asn	Thr	Gly	Ile	
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Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
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 Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
 305 310 315 320
 Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Pro Tyr
 325 330 335
 Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
 340 345 350
 Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser
 355 360 365
 Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
 370 375 380
 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
 385 390 395 400
 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
 405 410 415
 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
 420 425 430
 Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
 435 440 445
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 Arg Pro Thr Cys Lys Glu Val Val Ser Arg Gly Asp Asp Tyr
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 <213> Saccharomyces sp.

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 20 25 30
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 35 40 45
 Lys Lys Lys Lys Ser Asn Val Lys Lys Ile Glu Leu Leu Phe Pro Asp

50					55					60						
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Leu	Gln	Arg	Thr	Thr	Asp	Glu	Glu	Ser	Arg	Tyr	Leu	Lys	Arg	Asp	Leu	
				85					90					95		
Glu	Arg	Ala	Glu	His	Trp	Asn	Asp	Val	Arg	Lys	Gly	Ala	Glu	Ile	His	
			100					105					110			
Arg	Arg	Val	Arg	Arg	Ala	Ile	Lys	Asp	Arg	Ile	Val	Pro	Gly	Met	Lys	
		115					120					125				
Leu	Met	Asp	Ile	Ala	Asp	Met	Ile	Glu	Asn	Thr	Thr	Arg	Lys	Tyr	Thr	
	130					135					140					
Gly	Ala	Glu	Asn	Leu	Leu	Ala	Met	Glu	Asp	Pro	Lys	Ser	Gln	Gly	Ile	
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Gly	Phe	Pro	Thr	Gly	Leu	Ser	Leu	Asn	His	Cys	Ala	Ala	His	Phe	Thr	
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Pro	Asn	Ala	Gly	Asp	Lys	Thr	Val	Leu	Lys	Tyr	Glu	Asp	Val	Met	Lys	
			180					185					190			
Val	Asp	Tyr	Gly	Val	Gln	Val	Asn	Gly	Asn	Ile	Ile	Asp	Ser	Ala	Phe	
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Thr	Val	Ser	Phe	Asp	Pro	Gln	Tyr	Asp	Asn	Leu	Leu	Ala	Ala	Val	Lys	
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225					230					235					240	
Thr	Asp	Ile	Gly	Glu	Ala	Ile	Gln	Glu	Val	Met	Glu	Ser	Tyr	Glu	Val	
				245				250						255		
Glu	Ile	Asn	Gly	Glu	Thr	Tyr	Gln	Val	Lys	Pro	Cys	Arg	Asn	Leu	Cys	
		260					265						270			
Gly	His	Ser	Ile	Ala	Pro	Tyr	Arg	Ile	His	Gly	Gly	Lys	Ser	Val	Pro	
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Ile	Val	Lys	Asn	Gly	Asp	Thr	Thr	Lys	Met	Glu	Glu	Gly	Glu	His	Phe	
	290					295					300					
Ala	Ile	Glu	Thr	Phe	Gly	Ser	Thr	Gly	Arg	Gly	Tyr	Val	Thr	Ala	Gly	
305					310					315					320	
Gly	Glu	Val	Ser	His	Tyr	Ala	Arg	Ser	Ala	Glu	Asp	His	Gln	Val	Met	
				325				330					335			
Pro	Thr	Leu	Asp	Ser	Ala	Lys	Asn	Leu	Leu	Lys	Thr	Ile	Asp	Arg	Asn	
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Asp	Glu	Val	Ala	Lys	Gln	Leu	Glu	Arg	Gln	Ala	Leu	Glu	Glu	Lys	Glu
65					70					75					80
Lys	Asp	Asp	Asp	Asp	Glu	Asp	Gly	Asp	Gly	Asp	Gly	Asp	Gly	Ala	Ala
				85					90					95	
Gly	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Arg	Gly	Pro	Arg	Val	Gln
			100						105				110		
Thr	Asp	Pro	Pro	Ser	Val	Pro	Ile	Cys	Asp	Leu	Tyr	Pro	Asn	Gly	Val
		115					120					125			
Phe	Pro	Lys	Gly	Gln	Glu	Cys	Glu	Tyr	Pro	Pro	Thr	Gln	Asp	Gly	Arg
	130					135					140				
Thr	Ala	Ala	Trp	Arg	Thr	Thr	Ser	Glu	Glu	Lys	Lys	Ala	Leu	Asp	Gln
145					150					155					160
Ala	Ser	Glu	Glu	Ile	Trp	Asn	Asp	Phe	Arg	Glu	Ala	Ala	Glu	Ala	His
				165					170					175	
Arg	Gln	Val	Arg	Lys	Tyr	Val	Met	Ser	Trp	Ile	Lys	Pro	Gly	Met	Thr
			180					185					190		
Met	Ile	Glu	Ile	Cys	Glu	Lys	Leu	Glu	Asp	Cys	Ser	Arg	Lys	Leu	Ile
	195						200					205			
Lys	Glu	Asn	Gly	Leu	Asn	Ala	Gly	Leu	Ala	Xaa	Pro	Thr	Gly	Cys	Ser
	210					215					220				
Leu	Asn	Asn	Cys	Ala	Ala	Xaa	Tyr	Thr	Pro	Asn	Ala	Gly	Asp	Thr	Thr
225					230					235					240
Val	Leu	Gln	Tyr	Asp	Asp	Ile	Cys	Lys	Ile	Xaa	Phe	Gly	Thr	His	Ile
				245					250					255	
Ser	Gly	Arg	Ile	Ile	Xaa	Cys	Ala	Phe	Thr	Val	Thr	Phe	Asn	Pro	Lys
			260					265					270		
Tyr	Asp	Ile	Leu	Leu	Lys	Ala	Val	Lys	Asp	Ala	Thr	Asn	Thr	Gly	Ile
		275					280					285			
Lys	Cys	Ala	Gly	Ile	Asp	Val	Arg	Leu	Cys	Asp	Val	Gly	Glu	Ala	Ile
	290					295					300				
Gln	Glu	Val	Met	Glu	Ser	Tyr	Glu	Val	Glu	Ile	Asp	Gly	Lys	Thr	Tyr
305					310					315					320
Gln	Val	Lys	Pro	Ile	Arg	Asn	Xaa	Asn	Gly	Xaa	Ser	Ile	Gly	Pro	Tyr
				325					330					335	
Arg	Xaa	Xaa	Ala	Gly	Lys	Thr	Val	Pro	Ile	Val	Lys	Gly	Gly	Glu	Ala

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Thr	Arg	Met	Glu	Glu	Gly	Glu	Val	Tyr	Ala	Ile	Xaa	Thr	Phe	Gly	Ser	
355					360					365						
Thr	Gly	Lys	Gly	Val	Val	His	Asp	Asp	Met	Glu	Cys	Ser	His	Tyr	Met	
370					375					380						
Lys	Asn	Phe	Asp	Val	Gly	His	Val	Pro	Ile	Arg	Leu	Pro	Arg	Thr	Lys	
385					390					395					400	
His	Leu	Leu	Asn	Val	Ile	Asn	Glu	Asn	Phe	Gly	Thr	Leu	Ala	Phe	Cys	
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Arg	Arg	Trp	Leu	Asp	Arg	Leu	Gly	Glu	Ser	Lys	Tyr	Leu	Met	Ala	Leu	
420					425					430						
Lys	Asn	Leu	Cys	Asp	Leu	Gly	Ile	Val	Asp	Pro	Xaa	Pro	Pro	Xaa	Cys	
435					440					445						
Asp	Ile	Lys	Gly	Ser	Tyr	Thr	Ala	Gln	Phe	Xaa	His	Thr	Ile	Leu	Cys	
450					455					460						
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<220>
 <223> Rat MetAP2

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			20					25					30		
Glu	Ala	Ala	Lys	Lys	Lys	Arg	Arg	Lys	Lys	Lys	Lys	Gly	Lys	Gly	Ala
		35					40					45			
Val	Ser	Ala	Gly	Gln	Gln	Glu	Leu	Asp	Lys	Glu	Ser	Gly	Thr	Ser	Val
	50					55					60				
Asp	Glu	Val	Ala	Lys	Gln	Leu	Glu	Arg	Gln	Ala	Leu	Glu	Glu	Lys	Glu
65					70					75				80	
Lys	Asp	Asp	Asp	Asp	Glu	Asp	Gly	Asp	Gly	Asp	Gly	Asp	Gly	Ala	Ala
				85					90					95	
Gly	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Lys	Arg	Gly	Pro	Arg	Val	Gln
			100					105					110		

Thr	Asp	Pro	Pro	Ser	Val	Pro	Ile	Cys	Asp	Leu	Tyr	Pro	Asn	Gly	Val	115	120	125
Phe	Pro	Lys	Gly	Gln	Glu	Cys	Glu	Tyr	Pro	Pro	Thr	Gln	Asp	Gly	Arg	130	135	140
Thr	Ala	Ala	Trp	Arg	Thr	Thr	Ser	Glu	Glu	Lys	Lys	Ala	Leu	Asp	Gln	145	150	155
Ala	Ser	Glu	Glu	Ile	Trp	Asn	Asp	Phe	Arg	Glu	Ala	Ala	Glu	Ala	His	165	170	175
Arg	Gln	Val	Arg	Lys	Tyr	Val	Met	Ser	Trp	Ile	Lys	Pro	Gly	Met	Thr	180	185	190
Met	Ile	Glu	Ile	Cys	Glu	Lys	Leu	Glu	Asp	Cys	Ser	Arg	Lys	Leu	Ile	195	200	205
Lys	Glu	Asn	Gly	Leu	Asn	Ala	Gly	Leu	Ala	Phe	Pro	Thr	Gly	Cys	Ser	210	215	220
Leu	Asn	Asn	Cys	Ala	Ala	His	Tyr	Thr	Pro	Asn	Ala	Gly	Asp	Thr	Thr	225	230	235
Val	Leu	Gln	Tyr	Asp	Asp	Ile	Cys	Lys	Ile	Asp	Phe	Gly	Thr	His	Ile	245	250	255
Ser	Gly	Arg	Ile	Ile	Asp	Cys	Ala	Phe	Thr	Val	Thr	Phe	Asn	Pro	Lys	260	265	270
Tyr	Asp	Ile	Leu	Leu	Lys	Ala	Val	Lys	Asp	Ala	Thr	Asn	Thr	Gly	Ile	275	280	285
Lys	Cys	Ala	Gly	Ile	Asp	Val	Arg	Leu	Cys	Asp	Val	Gly	Glu	Ala	Ile	290	295	300
Gln	Glu	Val	Met	Glu	Ser	Tyr	Glu	Val	Glu	Ile	Asp	Gly	Lys	Thr	Tyr	305	310	315
Gln	Val	Lys	Pro	Ile	Arg	Asn	Leu	Asn	Gly	His	Ser	Ile	Gly	Pro	Tyr	325	330	335
Arg	Ile	His	Ala	Gly	Lys	Thr	Val	Pro	Ile	Val	Lys	Gly	Gly	Glu	Ala	340	345	350
Thr	Arg	Met	Glu	Glu	Gly	Glu	Val	Tyr	Ala	Ile	Glu	Thr	Phe	Gly	Ser	355	360	365
Thr	Gly	Lys	Gly	Val	Val	His	Asp	Asp	Met	Glu	Cys	Ser	His	Tyr	Met	370	375	380
Lys	Asn	Phe	Asp	Val	Gly	His	Val	Pro	Ile	Arg	Leu	Pro	Arg	Thr	Lys	385	390	395
His	Leu	Leu	Asn	Val	Ile	Asn	Glu	Asn	Phe	Gly	Thr	Leu	Ala	Phe	Cys	405	410	415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
435 440 445

Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Glu His Thr Ile Leu Cys
450 455 460

Ala Gln Pro Val Lys Lys Leu Ser Ala Glu Glu Met Thr Ile Lys Thr
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<210> 18

<211> 1944

<212> DNA

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<223> Rat MetAP2 variant

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<221> misc_feature

<222> (779)

<223> Any nucleotide

<400> 18

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aggaagccgc caagaagaaa agacggaaga agaagaaggg caaaggggct gtgtcagcag 240
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gacaagagtg tgaataccca cccacccaag atgggcggac agctgcttgg agaaccacaa 540
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 <212> PRT
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<220>
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 transit peptide

<400> 19
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<210> 20
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<210> 23
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<213> Artificial Sequence

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<220>
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